# Complete Summary

## GUIDELINE TITLE

Venous thromboembolism.

## BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Feb. 91 p. [202 references]

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Apr. 99 p.

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Venous thromboembolism (VTE)

### GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Prevention
Risk Assessment
Treatment

## CLINICAL SPECIALTY

Cardiology
Family Practice
Hematology
Internal Medicine
Pulmonary Medicine
Radiology
Vascular Surgery

## INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

## GUIDELINE OBJECTIVE(S)

- To prevent progression or recurrence of thromboembolic disease
- To reduce the risk of complications from anticoagulation therapy
- To improve quality of care and cost-effectiveness of the diagnosis and treatment of venous thromboembolism (VTE)

## TARGET POPULATION

Adult patients age 18 and over with venous thromboembolism (VTE)

Note: The treatment guidelines are not intended for patients with familial bleeding disorders.

## INTERVENTIONS AND PRACTICES CONSIDERED

### Diagnosis/Evaluation of Deep Vein Thrombosis (DVT)

1. Clinical evaluation, examination, and patient history
2. Clinical pretest probability model (protocol) of deep vein thrombosis (DVT), such as the Well's Model
3. D-dimer assays, such as enzyme linked immunoassay (ELISA); rapid ELISA (VIDAS®); and SimpliRED®
4. Venous duplex ultrasound with compression
5. Serial compression ultrasounds

6. Computed tomography (CT) venography of the iliac and vena cava
7. Contrast venography (proximal, intra-abdominal)
8. Magnetic resonance imaging (MRI)

Note: Magnetic resonance imaging is considered experimental for the diagnosis of deep vein thrombosis.

### Diagnosis/Evaluation of Pulmonary Embolism (PE)/Risk Assessment

1. Assessment of patient's clinical signs and symptoms, such as dyspnea, pleuritic chest pain, and tachypnea
2. Patient history and physical examination, including risk factor assessment for venous thromboembolism (VTE)
3. Laboratory evaluation, including chest x-ray; arterial blood gasses; and electrocardiogram (ECG)
4. Clinical pretest probability model for predicting probability of pulmonary embolism
5. Echocardiography
6. Ventilation/perfusion (V/Q) lung imaging
7. Helical computed tomographic pulmonary angiography (CTPA)
8. Duplex ultrasound with compression
9. D-dimer (ELISA or automated luminescence immunoassay [LIA])

### Treatment/Management/Prevention

1. Anticoagulation with warfarin
2. Low molecular weight heparin (LMWH), such as enoxaparin (Lovenox®), tinzaparin (Innohep®), dalteparin (Fragmin®)
3. Unfractionated heparin (UFH)
4. Baseline and periodic platelet counts during heparin therapy
5. Patient education on the use of anticoagulation
6. Graded compression stockings
7. Inferior vena cava (IVC) filters
8. Direct thrombin inhibitors such as lepirudin (Refludan®), argatroban (Acova®) and bivalirudin (Angiomax®) for treatment of heparin-induced thrombocytopenia
9. Activated partial prothromboplastin time (aPPT) monitoring during direct thrombin inhibitor therapy
10. Intravenous (IV) thrombolytic therapy
11. Surgical thrombectomy

## MAJOR OUTCOMES CONSIDERED

- Sensitivity, specificity, positive/negative predictive value, and utility of diagnostic tests
- Patient signs and symptoms
- Patient response to treatment
- Recurrence of thrombosis
- Complications of treatment (e.g., bleeding, heparin-induced thrombocytopenia)

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Additional descriptions of literature search strategies are not available.

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system presented below, and are designated as positive, negative, or neutral to reflect the study quality.

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results

from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

Study Quality Designations:

The quality of the primary research reports and systematic reviews are designated in the following ways on the conclusion grading worksheets:

Positive: indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.

Negative: indicates that these issues (inclusion/exclusion, bias, generalizability, and data collection and analysis) have not been adequately addressed.

Neutral: indicates that the report or review is neither exceptionally strong nor exceptionally weak.

Not Applicable: indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

Classes of Research Reports:

A. Primary Reports of New Data Collection:

   Class A:

   - Randomized, controlled trial

   Class B:

   - Cohort study

   Class C:

   - Non-randomized trial with concurrent or historical controls
   - Case-control study
   - Study of sensitivity and specificity of a diagnostic test
   - Population-based descriptive study

   Class D:

   - Cross-sectional study
   - Case series
   - Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

   Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

The guideline developers reviewed published cost analyses.

## METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline draft, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member medical groups during an eight-week period of "Critical Review."

Each of the Institute's participating medical groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating medical groups following general implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

### Guideline Work Group: Second Draft

Following the completion of the "Critical Review" period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary and a written response is prepared to address each of the suggestions received from medical groups. Two members of the Cardiovascular Steering Committee carefully review the Critical Review input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of two questions: (1) Have the concerns of the medical groups been adequately addressed? (2) Are the medical groups willing and able to implement the guideline? The committee then either approves the guideline for pilot testing as submitted or negotiates changes with the work group representative present at the meeting.

### Pilot Test

Medical groups introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and other practice systems. Evaluation and assessment occurs throughout the pilot test phase, which usually lasts for three months. Comments and suggestions are solicited in the same manner as used during the "Critical Review" phase.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Cardiovascular Steering Committee reviews the revised guideline and approves it for implementation.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): In addition to updating their clinical guidance, ICSI has developed a new format for all guidelines. Key additions and changes include: combination of the annotation and discussion section; the addition of "Key Points" at the beginning of most annotations; the inclusion of references supporting the recommendations; and a complete list of references in the Supporting Evidence section of the guideline. For a description of what has changed since the previous version of this guidance, refer to "Summary of Changes -- February - 2006."

The recommendations for venous thromboembolism are presented in the form of four algorithms, accompanied by detailed annotations. Algorithms on Deep Vein Thrombosis (DVT) Diagnosis; Pulmonary Embolism (PE) Diagnosis; V/Q (Ventilation/Perfusion) Lung Imaging; and Venous Thromboembolism (VTE) Treatment are provided. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) ratings and key conclusion grades (I-III, Not Assignable) are defined at the end of the "Major Recommendations" field.

## Clinical Highlights and Recommendations

1. Confirm diagnosis of DVT with imaging study, preferably duplex ultrasound (with compression). (Annotation #13)
2. A clinical pretest probability assessment should be completed in patients with suspected venous thromboembolism. (Annotations #2, 15)
3. D-dimer can be used as a negative predictor to eliminate need for further testing. (Annotations #4,10)
4. In patients with a high clinical pretest probability for PE, begin low-molecular-weight heparin (LMWH) without delay. (Annotation #15)
5. Achieve rapid effective anticoagulation with LMWH. (Annotation #60)
6. In patients with acute VTE, heparin (unfractionated heparin [UFH] or LMWH) should be given for at least four days and until the international normalized ratio (INR) is 2.0 for two consecutive times. (Annotation #61)
7. Graded compression stockings help prevent post-phlebotic syndrome. All patients should be assessed for the need for compression graded stockings. (Annotation #68)
8. Arrange for home therapy in appropriate patients. (Annotation #64)

## Deep Vein Thrombosis (DVT) Diagnosis Algorithm Annotations

1. Leg Symptoms/Clinical Suspicion of DVT

   Key Points:

   - Clinical evaluation and examination and patient history are important to the diagnosis of DVT.
   - Clinical findings alone are poor predictors of the presence or severity of thrombosis.

   Among patients with pain and swelling of the leg, some will have DVT. Recent unilateral swelling and pain above or below the knee without explanatory bone or joint trauma is suspicious for DVT.

   As part of the evaluation, record onset, location, and character of patient's leg pain and swelling.

   Factors increasing risk include:

   - Patient's history of past VTE, family history of VTE
   - Pregnancy, post partum, or current estrogen use

- Recent trauma or surgery
- Immobilization
- Presence of cancer
- Varicosities
- Airline flight longer than 8 hours

Exam findings may include erythema, warmth, and superficial thrombophlebitis with a palpable tender cord over a superficial vein. In the most severe form, phlegmasia cerulea dolens, the venous drainage of the lower extremity is acutely and severely obstructed threatening limb viability. This may require other treatment (see Annotation # 69, "Other Therapies.")

It is well known that clinical findings are poor predictors of the presence or severity of thrombosis; therefore, determining Pretest Probability is necessary in managing the diagnostic process.

The work group feels that patients who also have signs and symptoms of PE should be evaluated according to the PE Diagnosis Algorithm. Please refer to Annotation #14, "Clinical Signs and Symptoms of PE."

Evidence supporting this recommendation is of classes: D, R

2. Determine Clinical Pretest Probability

Key Points:

- Use a formal protocol to determine a patient's clinical pretest probability of DVT.

The work group recommends the use of a formal protocol to determine a patient's pretest probability of DVT. This can guide the choice of test(s) needed to triage patients for this condition, which can have minimal signs and symptoms but lead to serious consequences if left untreated. Please refer to Annotation Appendix A, "Well's Model of the Clinical Pretest Probability of DVT" in the original guideline document for an example of a clinical pretest probability model protocol.

Evidence supporting this recommendation is of class: B

3. Low Clinical Pretest Probability

Key Points:

- Patients with low clinical pretest probability of DVT and negative D-dimer are considered to have DVT ruled out and no further testing is needed.

Patients with a low clinical pretest probability of DVT such as those with a score of zero on Well's scoring can be safely managed by testing for D-dimer before ordering duplex ultrasound (with compression) of the leg. If D-dimer is negative, ultrasound can be omitted, and repeat ultrasound is not needed in

one week as previously recommended unless new or progressive clinical symptoms occur.

Evidence supporting this recommendation is of class: C

4. D-dimer Test

Key Points:

- D-dimer assays with a high sensitivity have been proven to have a strong negative predictive value for patients with a low pretest probability of DVT and PE.
- D-dimer tests are most appropriate in ambulatory care settings for patients with recent onset of symptoms.

D-dimer testing is most appropriate in ambulatory care settings and for patients with recent onset of symptoms who are not currently on anticoagulation therapy. For patients with suspected DVT, D-dimer may decrease the need for initial and subsequent radiological investigation. The usefulness is dependent on the method used for D-dimer determination [Conclusion Grade II: See Conclusion Grading Worksheet -- Appendix A -- Annotations #4 and 10 (DVT D-dimer) in the original guideline document].

Refer to the original guideline document for more information about D-dimer.

Evidence supporting this recommendation is of class: C

6. DVT Excluded - Out of Guideline

Patients with a low clinical pretest probability of DVT and a negative (reliable) D-dimer assay have a very low (less than 2%) risk of subsequent finding of DVT. These patients can be followed clinically with no further radiologic evaluation unless warranted by new or progressive clinical symptoms.

Evidence supporting this recommendation is of class: C

7. Moderate/High Clinical Pretest Probability

Key Points:

- Patients with moderate or high clinical pretest probability should have a venous Duplex ultrasound (with compression) ordered as the first test.
- D-dimer assay can be used after a negative duplex ultrasound (with compression) result to determine further radiologic testing needs.

Patients with moderate or high clinical pretest probability have a 15 to 70% risk of DVT. Because of the high incidence of DVT in this population, venous duplex ultrasound (with compression) should be ordered as the first test, and D-dimer assay can be used after a negative ultrasound result to determine further radiologic testing needs.

8. Perform Duplex Ultrasound (with Compression)

Key Points:

- Duplex ultrasound (with compression) is considered to be the primary diagnostic device and should be the first radiologic choice for evaluation of proximal DVT.
- The combined use of clinical pretest probability and duplex ultrasound (with compression) is effective in confirming or excluding the diagnosis of DVT.
- Duplex ultrasound (with compression) can find thrombi in the calf; however, a negative test cannot always exclude DVT and further testing may be needed.

Patients with a low clinical pretest probability of DVT and a positive D-dimer assay should receive a duplex ultrasound (with compression) to confirm the diagnosis of DVT. The ability to diagnose DVT may vary depending on the proximity of the suspected DVT site. In addition, the interpretation of the duplex ultrasound can be difficult in patients with a previous history of DVT. Consider consulting with the interpreting physician. (See Annotation #12, "Follow-Up Studies/Second Doppler Ultrasound (3-7 Days) or Venography.")

Patients with a moderate/high clinical pretest probability of DVT should receive a duplex ultrasound (with compression) as the first test to diagnose DVT. A negative result on the venous ultrasound can be followed by D-dimer to determine further radiologic testing needs. A positive result on the ultrasound confirms the diagnosis of DVT.

Proximal (popliteal vein and above)

Duplex ultrasound (with compression) is considered to be the primary diagnostic device and should be the first choice for evaluation.

Calf (below popliteal vein)

Some calf thrombi can be found by duplex ultrasound (with compression). However, a negative test cannot exclude an isolated calf DVT.

Evidence supporting this recommendation is of classes: A, B, C, R

10. D-dimer Test for Moderate/High Pretest

Key Points:

- It has been found safe to withhold anticoagulation in outpatients with a moderate to high clinical suspicion, a negative duplex ultrasound, and a negative D-dimer.

It is safe to withhold anticoagulation among outpatients with a negative duplex ultrasound (with compression) and a "negative" D-dimer (measured

by whole blood latex agglutination or enzyme-linked immunosorbent assay [ELISA], respectively).

For patients with suspected DVT, D-dimer testing may decrease the need for initial and subsequent radiological investigation. The usefulness is dependent on the method used for the D-dimer determination. [Conclusion Grade II: See Conclusion Grading Worksheet -- Appendix A -- Annotations #4 and #10 (DVT D-dimer) in the original guideline document.]

Evidence supporting this recommendation is of classes: B, C

12. Follow-Up Studies/Second Duplex Ultrasound (3-7 Days) or Venography

Key Points:

- If DVT is strongly suspected and there is a positive D-dimer despite a negative initial ultrasound, consider venography or repeat ultrasound in 3-7 days.

Clinical pretest probability and venous duplex ultrasound are adequate to rule in or rule out DVT in the majority of cases. If DVT is strongly suspected despite a negative initial ultrasound, consider venography or repeat ultrasound in 3 to 7 days. Please refer to Annotation Appendix A, "Wells Model of the Clinical Pretest Probability of DVT," in the original guideline document.

The combined use of clinical pretest probability and duplex ultrasound (with compression) is effective in confirming or excluding the diagnosis of DVT in the majority of cases. If clinical suspicion of DVT is high and ultrasound is negative, consider further testing, such as repeat ultrasound for suspected calf thrombosis or venography for suspected proximal thrombosis. [Conclusion Grade I: See Conclusion Grading Worksheet -- Appendix B -- Annotation #12 (DVT Diagnosis Confirmation) in the original guideline document.]

- Serial ultrasonography

  When calf thrombosis is suspected but the initial ultrasound is negative, serial ultrasound is an acceptable alternative to venography. Ultrasonography appears to be superior to impedance plethysmography for this purpose. If a thrombus is discovered, anticoagulation is recommended.

- Computed tomography (CT) venography of the inferior vena cava and the iliac veins is performed at some institutions to visualize proximal obstructions. The common, superficial, and deep femoral veins can be done as well. CT venography does not include the distal calf veins. Newer techniques include spiral contrast CT and magnetic resonance (MR) venography, which have shown excellent results in preliminary studies. This effectiveness has included iliocaval thrombi. Currently these techniques could be considered in patients with unusual

diagnostic situations including suspected iliocaval clots or in patients with contraindications for venography
- Contrast venography (proximal, intra-abdominal) is generally considered the historical gold standard for the accurate diagnosis. However, it has numerous drawbacks including cost, discomfort to the patient, significant resource use, availability, requirement of foot vein cannulation, use of intravenous (IV) contrast, and secondary thrombi. For these reasons, venography is generally reserved for difficult diagnostic cases. It can help distinguish between old and new clots.
- Magnetic Resonance Imaging (MRI) - experimental

Evidence supporting this recommendation is of classes: A, C, R

13. DVT Confirmed - See Venous Thromboembolism (VTE) Treatment Algorithm

Key Points:

- Proximal thrombosis should be treated with anticoagulation unless contraindicated.
- Thrombosis of the calf veins is common and carries significant risk of propagation. Patients benefit from anticoagulation treatment.
- Patients with thrombosis of the calf not treated with anticoagulation should be followed by serial duplex ultrasound to rule out proximal progression.

Proximal Thrombosis (at or above the popliteal vein)

Proximal thrombosis should be treated with anticoagulation unless contraindicated. (See Annotation #59, "Complicated VTE or Comorbidities?") Additional information can also be found in the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) Anticoagulation Therapy Supplement.

Calf Thrombosis (below the popliteal vein)

Increasing evidence suggests that patients with symptomatic calf DVT benefit from treatment similar to that for proximal DVT. Thrombosis of the calf veins is common and carries significant risk of propagation, including propagation into the proximal deep veins. If not treated, these patients should be followed by serial duplex ultrasounds to rule out proximal progression of thrombus to popliteal vein.

Following patients with suspected thrombosis limited to the calf veins and treating with anticoagulation only for proximal extension on serial studies may be an acceptable alternative to anticoagulation. However, the safety of this approach in patients with confirmed symptomatic calf DVT has not been studied.

Evidence supporting this recommendation is of classes: A, C, D, R

## Pulmonary Embolism (PE) Diagnosis Algorithm Annotations

14. Clinical Signs and Symptoms of PE

Key Points:

- PE should be considered in patients that present with the three most frequent signs and symptoms -- dyspnea, pleuritic chest pain, and tachypnea.

PE should be considered in patients that present with the three most frequent signs and symptoms: dyspnea, pleuritic chest pain, and tachypnea. Less frequent signs/symptoms are cough, hemoptysis, fever, syncope, diaphoresis, nonpleuritic chest pain, apprehension, rales, increased pulmonic component of the second heart sound ($\hat{S}_2P$), wheezing, hypotension, tachycardia, cyanosis, or pleural rub. Massive pulmonary embolism can present with hemodynamic instability or cardiac arrest. Clinical findings are nonspecific and should not be used as the only criteria to diagnose PE.

Evidence supporting this recommendation is of classes: C, R

15. Estimate Clinical Pretest Probability

Key Points:

- If high-risk, begin heparin without delay.
- Chest x-ray (CXR), arterial blood gases (ABGs), electrocardiogram (EKG), and other tests as indicated for alternative diagnoses considered.

If high-risk, begin LMWH without delay

Patients presenting with signs and symptoms of PE need:

- Complete history and physical exam. Risk factor assessment for venous thromboembolic disease plays a role in determining the pretest probability of PE. Risk factors include previous history of venous thromboembolism, recent surgery, immobilization, paresis, personal or family history of inheritable thrombophilic disorder or personal history of acquired thrombophilia (e.g. antiphospholipid antibody, cancer, estrogen, pregnancy or myeloproliferative disorder).
- Risk factor assessment (pretest probability). If high-risk, begin heparin promptly (a tool for determining pretest probability is shown in annotation Appendix B, "Model for Predicting Clinical Pretest Probability of PE" in the original guideline document).
- CXR, ABGs, EKG and other tests as indicated for alternative diagnoses considered
- Patients who present signs and symptoms of massive PE (syncope, hypotension, tachycardia, and hypoxia) may require evaluation and treatment different than that recommended in this guideline. In patients with suspected massive PE, echocardiography can be used as

a diagnostic and management tool. Please refer to Annotation #59, "Complicated Venous Thromboembolism or Comorbidities" in the Venous Thromboembolism Treatment Algorithm.

A simplified clinical pretest probability scoring system may improve diagnostic accuracy by being easy to use consistently and alerting clinicians to the need for further testing.

Refer to the original guideline document for more information.

Evidence supporting this recommendation is of classes: B, C, R

19. PE Ruled Out/Clinical Follow-Up, Consider Other Diagnoses

Key Points:

- It is important to evaluate patients for other diagnosis when PE has been excluded.

Patients with a negative D-dimer and low clinical pretest probability have a low incidence of pulmonary embolism. It is safe to withhold anticoagulation therapy and follow these patients clinically.

Patients who have had PE excluded need to have the evaluation for other diagnoses completed and appropriate treatment and followed-up initiated. In particular, pericarditis, myocardial infarction, and pneumonia should be excluded in the appropriate circumstances. When performed, computed tomographic pulmonary angiography (CTPA) will frequently help identify alternative causes such as pericardial effusion, pneumonia, pleural effusion, etc.

Evidence supporting this recommendation is of classes: B, C, R

22. Perform Computed Tomographic Pulmonary Angiography (CTPA)

Key Points:

- Non-invasive pulmonary vascular imaging studies are recommended as the initial radiologic evaluation.

Current practice is to choose between two methods to image the pulmonary blood vessels:

A. CT pulmonary angiography
B. Ventilation/perfusion (V/Q) scan

The choice of initial imaging study depends on several factors including how readily available the tests are, the resolution of images obtained, underlying illnesses of the patient, and experience of the radiologists.

Non-invasive pulmonary vascular imaging studies are recommended as the initial diagnostic evaluation in most patients with suspected PE. Both V/Q scans and CT pulmonary angiography have a relatively high degree of specificity when they are read respectively as "high probability" scan results or "positive" for PE. A negative V/Q scan also has a high degree of specificity. However, either a non-diagnostic (intermediate or low radiologic probability scan results) or a negative CT pulmonary angiogram suffer from lack of sensitivity and usually require further diagnostic studies. V/Q scanning is the most studied form of non-invasive lung imaging. It is not always readily available and other pulmonary processes such as chronic obstructive pulmonary disease (COPD) and congestive heart failure can influence its specificity.

Evidence supporting these recommendations is of classes: C, R

24. CT Pulmonary Angiography Positive?

Key Points:

- CT pulmonary angiography has become the most commonly used radiographic test to be used to evaluate patients for PE.

CT pulmonary angiography offers the clinician a new screening tool for detection of pulmonary embolism. It has been rapidly introduced into clinical practice and, in some institutions, is easier to obtain than a V/Q scan. CT pulmonary angiography is also more useful in patients with underlying cardiac disease and COPD/asthma. When alternative diagnoses are likely, CT pulmonary angiography is especially good as it can rule out PE and confirm other diagnoses with one test.

Refer to the original guideline document for more information regarding CT pulmonary angiography.

Evidence supporting this recommendation is of classes: M, R

25. Perform D-dimer and Assess Pretest Probability

Key Points:

- In patients with moderate clinical pretest probability and negative CTPA and D-dimer, PE can be ruled out.

Moderate Clinical Pretest Probability

Patients with a negative CT pulmonary angiography but moderate clinical pretest probability have a small but significant incidence of pulmonary embolism.

Follow-up studies such as D-dimer testing or ultrasounds are recommended to improve the diagnostic sensitivity for pulmonary emboli while avoiding

invasive diagnostic tests. Please refer to Annotation #10, "D-dimer Test for Moderate/High Pretest."

High Clinical Pretest Probability

A significant incidence of PE is found in patients with a negative CT pulmonary angiography associated with a high clinical pretest probability. Bilateral duplex ultrasound (with compression) of the leg is recommended to improve the diagnosis of VTE without performing invasive tests. Pulmonary angiography is recommended.

27. Low/Moderate Clinical Pretest Probability and Positive D-dimer or High Clinical Pretest Probability and Negative D-dimer

Key Points:

- Further evaluation with either ultrasonography or a D-dimer with sufficient negative predictive value is suggested in this patient population with significant incidence of thromboembolism.

It appears to be safe to withhold anticoagulation while pursuing a non-invasive strategy of serial ultrasonography in order to further evaluate for thromboembolism in this patient population.

Patients with a negative CTPA and either a moderate pretest probability with a positive D-dimer or a high pretest probability with a negative D-dimer have an unclear diagnostic picture and further testing is recommended. Consider bilateral ultrasound or angiogram testing.

The risks associated with a misdiagnosis of PE are typically more severe than those associated with a misdiagnosis of DVT. Higher negative predictive values are required to safely use D-dimer to exclude PE. The evidence, to date, suggests that current assays, with the possible exception of ELISA and rapid ELISA methods, are not acceptable for use in excluding PE in patients with clinical suspicion of PE. [Conclusion Grade III: See Conclusion Grading Worksheet -- Appendix C -- Annotation #27 (Perform D-dimer and Assess Clinical Pretest Probability) in the original guideline document]

Evidence supporting this recommendation is of class: C

29. Perform Duplex Ultrasound (with Compression) of the Leg

Key Points:

- Duplex ultrasound (with compression) should be used to improve clinical likelihood of disease and avoid more invasive testing in patients with negative lung imaging results.

In patients with non-diagnostic V/Q scans or negative CT pulmonary angiography results, further evaluation with duplex ultrasound (with compression) should be used to improve clinical likelihood of disease and

avoid more invasive testing. Please refer to Annotation Appendix C in the original guideline document for sample ultrasound orders.

The diagnosis of lower extremity deep vein thrombosis has been advocated to be an important adjunct to the diagnosis of pulmonary emboli. Venous duplex ultrasonography (DUS) is the most common method for DVT diagnosis. DUS accuracy for lower extremity DVT is as high as 98%, though studies are negative in greater than 50% of pulmonary embolism cases. Total thrombus embolism and proximal migration may account for a number of negative studies. Venous DUS reliability is also limited when evaluating iliac and pelvic veins and the inferior vena cava, which likely accounts for a significant number of negative studies.

When DUS is negative, the incorporation of clinical pretest probability can improve diagnostic accuracy and potentially avoid unnecessary pulmonary angiography. Several studies of DUS performed after nondiagnostic V/Q scans have shown that pulmonary angiography can be avoided in 15% to 40% of patients when DVT is identified.

Clinical pretest probability is an important adjunct to DUS at this point. In cases of suspected pulmonary embolism where non-invasive tests do not confirm its presence, pulmonary angiography should be performed.

Evidence supporting this recommendation is of classes: C, D, M

30. Ultrasound Positive?

A positive ultrasound usually confirms the diagnosis of DVT and requires treatment regardless of the presence or absence of PE. If the ultrasound is negative, further evaluation may be warranted, dependent upon the patient's clinical pretest probability.

34. Angiogram Positive?

Key Points:

- Pulmonary angiography is considered the diagnostic reference standard for the diagnosis of pulmonary embolism.

Pulmonary angiography is considered the diagnostic reference standard for the diagnosis of pulmonary embolism and is indicated when there is significant doubt about a diagnosis of pulmonary embolism after non-invasive studies. It is often performed when lung scan results are non-diagnostic or when the results are at odds with the clinical impression. An angiogram is generally safe and well-tolerated in selected patients. Benefits outweigh the risks when a definitive diagnosis is necessary.

When there is a high clinical suspicion of pulmonary embolism, angiography is indicated, despite negative lower extremity evaluation and negative CT results. In situations where the clinical suspicion is high but CT scan is negative, pulmonary angiography is indicated based upon noninvasive study

results. Angiography may provide additional differential diagnostic information.

Evidence supporting this recommendation is of classes: B, C, D

35. Diagnosis of PE

Patients with a positive CTPA scan and moderate or high clinical pretest probability are essentially confirmed positive for PE. They can be considered for treatment with no further diagnostic testing.

Evidence supporting this recommendation is of classes: B, C, R

## V/Q Lung Imaging Algorithm Annotations

37. Ventilation/Perfusion (V/Q) Lung Imaging

Key Points:

- Normal and high probability scans are considered diagnostic unless the clinical probability strongly suggests otherwise.
- Low, intermediate and indeterminate readings are considered non-diagnostic and further testing is usually required.
- CT may be the preferred modality in all patients in the proper clinical setting (no renal failure and technical expertise in CT scanning for PE).
- V/Q scan may be most appropriate for patients with contrast allergies or renal insufficiency.

The phraseology of V/Q classification has generated confusion. Low probability scans are not really low clinical probability for PE. Up to 25% of these patients have PE on angiogram. Approximately 40% of patients with intermediate (non-diagnostic) scans have positive angiograms. Thus, these two groups of scans are more properly considered non-diagnostic scans and require further evaluation. In the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED), 72% of enrolled patients had non-diagnostic scans. All these patients required further evaluation. In general, normal and high probability scans are considered diagnostic unless the clinical probability strongly suggests otherwise. Low, intermediate and indeterminate readings are considered non-diagnostic and have a probability of PE that ranges from about 15% to 40%. Further testing is usually required. When a contrast load needs to be avoided, such as in patients with renal insufficiency or dye allergy, the V/Q scan is preferred.

High probability scans are associated with PE approximately 90% of the time, and unless the clinical situation does not fit, can be considered positive.

Evidence supporting this recommendation is of classes: B, C

38. V/Q Normal

A normal perfusion scan, irrespective of ventilation abnormalities, essentially excludes the diagnosis of PE.

Evidence supporting this recommendation is of classes: D, R

40. V/Q Non-Diagnostic (Low or Intermediate Scan Results)

Key Points:

- Patients with a non-diagnostic V/Q scan have an incidence of pulmonary embolism that varies from 15% to 40%. Further diagnostic studies are recommended.

Radiologists typically report non-diagnostic scans as either low probability or intermediate probability. Low probability scans are associated with positive angiograms 15% to 25% of the time. Intermediate probability scans are associated with positive angiograms 30% to 40% of the time. Therefore, clinicians currently designate these as non-diagnostic scans. Further diagnostic testing combined with the clinical pretest probability will help determine the final diagnosis.

Evidence supporting this recommendation is of class: C

41. V/Q Diagnostic (High Probability Scan Result)

Key Points:

- A high probability (diagnostic) V/Q scan and the clinical suspicion is intermediate or high, this test can be considered a final diagnostic test.
- A high probability (diagnostic) V/Q scan and the clinical suspicion is actually low, one may consider further evaluation with a CT pulmonary angiogram.

The significance of a high probability (diagnostic) V/Q scan depends on the clinical pretest probability of PE. Several clinical studies have demonstrated that high probability scans are associated with PE at least 85% of the time. If the clinical suspicion is intermediate or high, this test can be considered a final diagnostic test. However, if the clinical suspicion is actually low, the incidence of pulmonary embolism appears to be 35% to 55%. In this circumstance, one should consider further evaluation with a CT pulmonary angiogram. A positive CT pulmonary angiogram in central pulmonary arteries has a high degree of specificity and may be considered diagnostic. A positive CT pulmonary angiogram in peripheral vessels may not represent a true positive finding. Depending upon the clinical pretest probability, the patient may need further work-up with a standard pulmonary angiogram.

In each patient with a high probability (diagnostic) V/Q scan, the clinician should consider whether this might represent a massive PE. If the patient also has hemodynamic changes or profound hypoxemia, one should consider whether the patient is a candidate for thrombolytic therapy. In this setting, an

echocardiogram evaluating right ventricular function can provide additional guidance for the use of thrombolytic therapy. (See Annotation #59, "Complicated Venous Thromboembolism or Comorbidities.")

Evidence supporting this recommendation is of classes: B, R

46. Assess Clinical Pretest Probability

Key Points:

- In patients with moderate or high clinical pretest probability, a high probability (diagnostic) V/Q scan can be considered the confirmatory test.
- In patients with low clinical pretest probability, the V/Q lung scan is frequently false positive.

In patients with low clinical pretest probability, the V/Q lung scan is frequently false positive. It is recommended that further studies be performed to confirm the positive V/Q finding. In this circumstance, pulmonary angiogram to rule in or out PE is the recommended procedure unless the patient has specific contraindications.

In patients with moderate or high clinical pretest probability, a high probability (diagnostic) V/Q scan has 85% to 90% sensitivity for PE and can be considered the confirmatory test. Proceed to the VTE Treatment Algorithm.

Refer to the original guideline document for more information on low, moderate, and high clinical pretest probability of PE.

Evidence supporting this recommendation is of class: B

47. Low Clinical Pretest Probability

Patients with a non-diagnostic V/Q scan associated with a negative duplex ultrasound with compression and low clinical pretest probability have a low incidence of pulmonary embolism. It is safe to withhold anticoagulation therapy and follow these patients clinically. Refer to Annotation #19, "PE Ruled Out/Clinical Follow-Up, Consider Other Diagnoses."

Evidence supporting this recommendation is of classes: B, C, R

50. High Clinical Pretest Probability

Key Points:

- A significant incidence of PE is found in patients with non-diagnostic V/Q scan associated with a negative duplex ultrasound with compression, but a high clinical pretest probability.
- Consider further testing (e.g., angiogram) in these patients.

A significant incidence of PE is found in patients with non-diagnostic V/Q scan associated with a negative duplex ultrasound, but a high clinical pretest probability. A positive ultrasound confirms the diagnosis of DVT, but a negative ultrasound cannot be used to exclude the diagnosis in this circumstance. Pulmonary angiography is recommended. Please refer to Annotation #34, "Angiogram Positive?"

Evidence supporting this recommendation is of classes: B, C, R

## Venous Thromboembolism (VTE) Treatment Algorithm Annotations

### 59. Complicated Venous Thromboembolism or Comorbidities?

Key Points:

- Patients with complicated venous thromboembolism or certain comorbidities may require therapy that is different than patients with uncomplicated venous thromboembolism. The work group felt that these patients should be identified and treated individually rather than by a standard guideline.
- Complications or comorbidities of venous thromboembolism include massive PE, contraindications to anticoagulation, known history of heparin-induced thrombocytopenia (HIT), extensive iliofemoral thrombosis/phlegmasia, pregnancy, familial bleeding and clotting disorders, and severe renal dysfunction.

Massive PE

Patients who present with symptoms of PE associated with hemodynamic or respiratory compromise should be evaluated for massive PE. These patients may require treatment other than that discussed in the guideline.

Massive PE should be considered in the following circumstances: any hemodynamic instability, severe hypoxemia or respiratory distress, a V/Q or angiogram with 50% of the perfusion absent, an echocardiogram showing right heart strain or failure, an elevated pulmonary artery pressure, or a spiral CT suggesting severe occlusion. Massive PE has up to a tenfold greater mortality and treatment with thrombolytics appears to favorably affect the outcome. A recent study has also suggested that there may be some benefit for the use of thrombolytics in submassive PE. In this circumstance, specialty consultation and consideration of thrombolytics may be appropriate.

Patients with hemodynamic compromise may require immediate thrombolytic therapy. Normotensive PE patients with right ventricle (RV) dysfunction should be treated in-hospital (at least initially) where their vital signs can be closely monitored. Such patients should be considered for thrombectomy (either catheter-directed or open), thrombolysis, and/or inferior vena cava (IVC) filter placement if blood pressure support (i.e., pressors and augmentation of intravascular volume) is required, and possibly if hypoxemia cannot be corrected with supplemental oxygen therapy.

Evidence supporting this recommendation is of classes: A, B, D, M, R

Contraindications to Anticoagulation

Absolute contraindications would include patients who have active severe hemorrhage or recent intracranial hemorrhage. Relative contraindications include: recent or imminent surgery, trauma, anemia (hematocrit less than 30), renal disease, history of gastrointestinal hemorrhage, active peptic ulcer disease, and liver disease.

These patients require more intense monitoring for bleeding complications if given anticoagulation therapy. If not treated with anticoagulation therapy, serial ultrasounds for untreated calf DVT, or IVC filters for proximal DVT are indicated. (See Annotation #69, "Other Therapies.") Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on contraindications to anticoagulation.

Evidence supporting this recommendation is of classes: A, B

Known History of Heparin-Induced Thrombocytopenia (HIT)

Thrombocytopenia can complicate heparin therapy. Both a non-immune and a more serious immune mediated platelet associated immunoglobulin G (IgG) reaction, HIT, have been described. If the patient has previously received heparin, especially within the past 3 months, thrombocytopenia may occur within hours or days.

Patients with HIT should not be treated with either unfractionated heparin (UFH) or low- molecular-weight heparin (LMWH). Direct thrombin inhibitors have been used successfully in this circumstance. (See Annotation # 69, "Other Therapies.") Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on HIT.

Evidence supporting this recommendation is of class: C

Extensive Iliofemoral Thrombosis/Phlegmasia

Patients found to have extensive iliofemoral disease or evidence of phlegmasia will likely require inpatient monitoring and longer course of heparin/LMWH therapy than patients with uncomplicated DVT. Thrombolytic therapy may be of benefit in these patients for possible reduction of post-thrombotic complications. (See Annotation # 69, "Other Therapies.")

Pregnancy

In pregnancy, warfarin (Coumadin®) is contraindicated because it crosses the placenta and is associated with embryopathy, central nervous system (CNS) abnormalities, and neonatal bleeding. Subcutaneous UFH, twice daily, has been the standard therapy in pregnancy. LMWH has shown no increased fetal complication, and was shown to have fewer bleeding complications than UFH.

Renal clearance of enoxaparin may be increased during pregnancy.

Anticoagulation will need to continue 4 to 6 weeks after delivery because the postpartum period is itself a high-risk time for thrombosis.

Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on anticoagulation therapy during pregnancy.

Evidence supporting this recommendation is of classes: A, D, M

Familial Bleeding Disorders

Because of the complexity and controversy surrounding the use of standard anticoagulation to treat DVT in patients with familial bleeding disorders, these patients are excluded from the guideline. There is little data that has addressed the use of low-molecular-weight heparin in these patients. Although treatment for these patients may be similar to that found in the algorithm, the work group felt that these patients should be treated individually and not be included in the guideline.

Severe Renal Dysfunction (creatinine clearance less than 30 mL/minute)

These patients require closer monitoring for bleeding complications and dosing adjustments if LMWH is used. Patients with significant renal impairment (creatinine clearance less than 30 mL/min) can accumulate LMWH. The recommended doses in these patients are currently:

- Enoxaparin (Lovenox®) 1 mg/kg ONCE daily for therapeutic (treatment) doses. (Normal renal function dose is 1 mg/kg twice daily or 1.5 mg/kg once daily)
- Enoxaparin (Lovenox®) 30 mg ONCE daily for prophylactic doses. (Normal renal function dose is 30 mg twice daily or 40 mg once daily)

Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on anticoagulation therapy in patients with renal dysfunction.

Evidence supporting this recommendation is of classes: B, C

60. Low-Molecular-Weight Heparin (LMWH)/Unfractionated Heparin (UFH)

Key Points:

- Unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) should be considered for the initial treatment of PE.
- LMWH is the preferred heparin for the initial anticoagulation for most patients with DVT.

- Heparin-induced thrombocytopenia (HIT) is a recognized complication of heparin therapy.

UFH or LMWH should be considered for the initial treatment of PE. LMWH is the preferred heparin for the initial anticoagulation of patients with DVT. It is as safe and as effective as continuous UFH. Suitable patients can be safely treated with LMWH in the outpatient setting. [Conclusion Grade I: See Conclusion Grading Worksheet -- Appendix D -- Annotation #60 (Low Molecular Weight Heparin) in the original guideline document]

Heparin should be continued for at least 5 days after the initiation of warfarin therapy and until INR is above 2.0 for two consecutive days.

Low-Molecular-Weight Heparin (LMWH)

Low-molecular-weight heparins provide reliable anticoagulation levels when given subcutaneously on a weight-determined dosing schedule. No laboratory monitoring of the intensity of anticoagulation is required for LMWH, except for special circumstances.

Please note LMWH may not be appropriate for patients with renal insufficiency (creatinine clearance less than 30 mL/min). (See Annotation #59, "Complicated Venous Thromboembolism or Comorbidities?")

- Enoxaparin (Lovenox®) 1.0 mg/kg subcutaneously twice daily is the recommended treatment for DVT (Food and Drug Administration [FDA] approved for inpatients and outpatients).
- Enoxaparin (Lovenox®) 1.5 mg/kg subcutaneously once daily (FDA approved for inpatient venous thromboembolism treatment). Risk factors for therapy failure with once-daily dosing include obesity (greater than 100 kg), cancer, and chronic kidney disease. Twice-daily dosing (enoxaparin 1mg/kg subcutaneously, twice daily) is recommended for obese patients and patients with cancer.
- Tinzaparin (Innohep®) 175 anti-Xa IU/kg subcutaneously once daily (FDA approved for venous thromboembolism treatment)
- Dalteparin (Fragmin®) 100 IU/kg subcutaneously twice daily (not FDA approved for venous thromboembolism treatment)
- Dalteparin (Fragmin®) 200 IU/kg subcutaneously once daily (The effectiveness of once-daily dosing is controversial) (not FDA approved for venous thromboembolism treatment)

LMWH is the preferred heparin for the initial anticoagulation of patients with DVT. It is as safe and as effective as continuous UFH. Suitable patients can be safely treated with LMWH in the outpatient setting. [Conclusion Grade I: See Conclusion Grading Worksheet -- Appendix D -- Annotation #60 (Low-Molecular- Weight heparin) in the original guideline document].

Studies of LMWH have generally excluded pregnant patients. However, neither unfractionated nor LMWH cross the placenta, and pregnant patients are suitable candidates for either form of therapy.

The decision for hospital or home therapy is not mutually exclusive. A patient could be started on LMWH in the hospital and discharged to continue therapy at home at any time during the course of therapy.

Evidence supporting this recommendation is of classes: A, B, C, R

Unfractionated Heparin (UFH)

UFH is administered by continuous IV infusion following a bolus dose. Heparin-induced thrombocytopenia is a recognized complication of UFH therapy. (See Annotation #69, "Other Therapies.")

Refer to the original guideline document for more information on UFH.

Evidence supporting this recommendation is of classes: A, C, R

Heparin-Induced Thrombocytopenia (HIT)

Both UFH and LMWH are associated with heparin-induced thrombocytopenia (HIT). HIT is an immune-mediated reaction to heparins. It occurs in 2% to 3% of patients treated with UFH and less than 1% of patients treated with LMWH. This syndrome can be associated with paradoxical increased risk for venous and arterial thrombosis. Patients who develop HIT without associated thrombosis will have a significant risk for thrombosis in the subsequent 100 days. Patients with a history of HIT should not be treated with UFH or LMWH.

HIT should be suspected in patients who develop a skin lesion reaction at the injection site, have a systemic reaction to a bolus administration of heparin, or develop a greater than 50% decrease in platelet count from baseline labs while on heparin. These patients should have their heparin stopped while antibody testing for HIT is performed. Patients with a high clinical probability of having HIT should be treated with an appropriate alternative anticoagulant before antibody test results are available. Direct thrombin inhibitors (DTIs) are the alternative anticoagulant of choice for patients with HIT. Three brands are FDA approved: lepirudin (Refludan®), argatroban, and most recently, bivalirudin (Angiomax®).

Although in vitro data has not demonstrated cross-reactivity of fondaparinux with HIT antibodies, additional studies are needed before its use can be considered.

Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on low molecular weight and unfractionated heparins, synthetic pentasaccharides, and HIT.

Evidence supporting this recommendation is of class: A

61. Warfarin

Key Points:

- A high-loading dose of warfarin (greater than 10 mg) is of no clinical use and should be discouraged.
- A 10 mg initial dose of warfarin has been associated with early over-anticoagulation and, when compared to a 5 mg initial dose, was no more effective in achieving a therapeutic INR by day 4 or 5 of therapy.
- A therapeutic range of anticoagulation to keep the INR at 2.5 (range 2.0 to 3.0) is recommended for patients with VTE.
- Heparin (UFH or LMWH) should be given for at least four days and until the INR is 2.0 two consecutive days.

It has been shown that oral anticoagulation with warfarin decreases the complications and recurrence rate of thrombosis.

It is recommended that warfarin therapy be initiated with a dose of 5 mg (less in patients with risks for increased sensitivity to warfarin) with dosage adjustments based on results of INR testing.

- A high-loading dose of warfarin (greater than 10 mg) is of no clinical use and should be discouraged. A high-loading dose induces a rapid but excessive reduction in Factor VII activity, predisposing patients to hemorrhage in the first few days of therapy. It fails to achieve a significantly more rapid decline of the other vitamin K dependent coagulation factors (II, IX and X) above that achieved without a loading dose.
- A 10 mg initial dose of warfarin has been associated with early over-anticoagulation and, when compared to a 5 mg initial dose, was no more effective in achieving a therapeutic INR by day 4 or 5 of therapy.

A therapeutic range of anticoagulation to keep the INR at 2.5 (range 2.0 to 3.0) is recommended for patients with VTE.

Refer to the original guideline document for more information.

Also, the NGC summary of the ICSI's Anticoagulation Therapy Supplement contains additional information on warfarin therapy including an appendix on interactions with warfarin.

Evidence supporting this recommendation is of classes: A, B, D, R

62. Outpatient Treatment Appropriate?

Key Points:

- Home therapy with LMWH is as safe and effective as in-hospital therapy with standard UFH for patients with uncomplicated VTE.
- Because of decreased cardiorespiratory reserve, patients presenting with symptomatic PE should initially be treated in-hospital.

Medical criteria for safe outpatient therapy include:

- Uncomplicated venous thromboembolism. (See Annotation #59, "Complicated Venous Thromboembolism or Comorbidities?")
- Good cardiorespiratory reserve
- No excessive bleeding risks
- Creatinine clearance greater than 30 mL/minute

Because of decreased cardiorespiratory reserve, patients presenting with symptomatic PE should initially be treated in-hospital.

Other considerations include:

- Patients need to be taught how to administer the drug and recognize complications.
- Daily INRs will be needed to guide the institution of warfarin therapy. The warfarin dose will need to be adjusted to the INR.
- Patients will need resources to answer questions and deal with problems.

Evidence supporting this recommendation is of classes: A, C

63. Inpatient Treatment

Therapy is discussed in Annotation #60, "Low-Molecular-Weight Heparin (LMWH)/Unfractionated Heparin (UFH)" and in Annotation # 61, "Warfarin."

64. Outpatient Protocol

Key Points:

- Patients may need hospitalization during the first 24 hours to start therapy promptly.
- Compression stockings (not Teds) combined with early ambulation does not cause any increase in pulmonary embolism and gives more rapid resolution of pain and swelling.

Because of the need for an organized support system and time of day considerations for home care agencies, many patients may need hospitalization during the first 24 hours to start therapy promptly.

All stable VTE patients

- Daily LMWH shots self-administered, caregiver-administered, or daily clinic visits. The patient will need to be geographically accessible to have INRs drawn and receive care for problems that arise.
- Daily INR for transitioning to warfarin treatment after 2 days of adequate anticoagulation. (For details see Anticoagulation Therapy Supplement)
- Duration of anticoagulation to be determined by the supervising physician.

DVT patients

- If the criteria in Annotation # 62 can be met, DVT treatment can be started in the outpatient setting; otherwise hospitalize until teaching, medication and close follow-up can be assured.
- For DVT use graduated compression stockings (not Teds) on the affected leg to reduce the risk of postphlebitic syndrome.
- Graded compression stockings (not Teds) combined with early ambulation does not cause any increase in pulmonary embolism and gives more rapid resolution of pain and swelling.

Please refer to the NGC summary of the ICSI's Anticoagulation Therapy Supplement for a discussion of complications during anticoagulation therapy.

Evidence supporting this recommendation is of classes: A, D

65. Patient Education

Patients should be instructed on the use of anticoagulation. Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on patient education. Patient education materials are also available. (See the Support for Implementation section in the original guideline document).

66. Complications During Therapy?

Key Points:

- Patients with complicated venous thromboembolism or certain comorbidities may require therapy that is different than patients with uncomplicated venous thromboembolism. These patients should be identified and treated individually rather than by a standard guideline.

Patients with complicated venous thromboembolism or certain comorbidities may require therapy that is different than patients with uncomplicated venous thromboembolism. These patients should be identified and treated individually rather than by a standard guideline.

Patients on UFH or LMWH therapy who have bleeding, thrombocytopenia, or osteoporosis may require individual adjustments in therapy. HIT should be suspected if the platelet count drops 50% or more from baseline labs.

Patients on warfarin therapy who experience bleeding or skin necrosis, or who become pregnant may require individual adjustments in therapy.

The development of a complication attributable to anticoagulation requires action by the health care team. Sometimes, as with heparin-induced thrombocytopenia (HIT), the drug must be discontinued. The most common complication, bleeding, may require a dosage adjustment, discontinuation of the drug, or further evaluation in the setting of gastrointestinal or genitourinary bleeding. Specific actions are best determined in a case-by-case basis by the clinician, who can appropriately weigh the risks and benefits of

continued anticoagulation therapy and who can take into account the timing of the complication.

Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on potential complications of anticoagulation therapy.

67. Anticoagulation Failure?

Key Points:

- Recurrent symptomatic DVT or PE during adequate heparin or warfarin treatment represents failure of treatment and needs objective documentation, especially as a new DVT may be difficult to distinguish from postphlebitic syndrome.
- If a patient fails on warfarin therapy, heparin or LMWH may need to be reinstituted.

Recurrent symptomatic DVT or PE during adequate heparin or warfarin treatment represents failure of treatment and needs objective documentation, especially as a new DVT may be difficult to distinguish from postphlebitic syndrome.

Active cancer is the most common cause of warfarin failure.

Antiphospholipid antibodies may be the cause of anticoagulant failure. In these patients, recurrence was most likely in the 6 months following cessation of warfarin, and higher INRs of greater than or equal to 3.0 were more effective than 2 to 3. Aspirin did not help.

In certain circumstances, alternate treatment such as an inferior vena cava filter may be indicated. If a patient fails on warfarin therapy, heparin or LMWH may need to be reinstituted. The work group felt these patients should be identified and treated individually rather than by a standard guideline. The 7th American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy provides the following recommendations regarding placement of an inferior vena cava (IVC) filter:

- For most patients with DVT, the work group recommends against the routine use of a vena cava filter in addition to anticoagulants.
- The work group suggests placement of an inferior vena cava filter in patients with a contraindication for or a complication of anticoagulant treatment, as well as in those with recurrent thrombophlebitis despite adequate anticoagulation.
- In PE patients with a contraindication for a complication of anticoagulant treatment as well as those with recurrent thromboembolism despite adequate anticoagulation, the work group suggests placement of an inferior vena cava filter.

Evidence supporting this recommendation is of classes: A, B, C, R

68. Continued Anticoagulation With Follow-Up and Secondary Prevention

Key Points:

- The length of anticoagulation therapy should be individualized to the patient and the circumstances that caused VTE.
- Patient who have had VTE remain at risk for recurrence for up to 10 years.

Graded Compression Stockings (not Teds)

Knee-high 30 to 40 mm Hg custom fitted, graded compression stockings help alleviate symptoms of edema and pain in patients who have postphlebitic syndrome. One report showed that graded compression stockings reduced the incidence of postphlebitic syndrome by 50% in patients with acute DVT. For chronic or recurrent venous stasis ulcer, consultation with a vascular surgeon should be considered.

Evidence supporting this recommendation is of classes: A, C, D

Duration of Anticoagulation

The most appropriate duration of warfarin anticoagulation should be individualized depending on the estimated risk of VTE recurrence and the risk of a complication (e.g., bleeding) due to warfarin therapy. The 7th American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy recommends:

- Transient risk (e.g., surgery, immobilization, estrogen use, trauma): 3 months. Shorter treatment periods are associated with a higher rate of recurrence and are not recommended.
- Idiopathic or medical risk: 6 to 12 months
    - Patients with documented antiphospholipid antibodies or two or more thrombophilic conditions should be treated for 12 months and considered for indefinite anticoagulation therapy.
    - Patients with documented deficiency of antithrombin, protein C or S, factor V Leiden, prothrombin 20210 mutation, homocysteinemia, or high factor VIII conditions should be treated for 6 to 12 months and considered for indefinite anticoagulation therapy.
- Recurrent disease or continued risk factors: indefinite
    - Patients with cancer should be treated for 3 to 6 months with LWMH and anticoagulation therapy indefinitely or until the cancer is resolved.
    - Patients with two or more episodes of documented DVT should receive anticoagulation therapy indefinitely.

Refer to the original guideline document for more information on duration of coagulation.

Evidence supporting this recommendation is of classes: B, R

## Anticoagulation Management

A coordinated effort for follow-up of patients started on warfarin is required to minimize the risks of both hemorrhagic and thrombotic complications while on treatment. In the first several weeks of anticoagulation, INRs need to be checked at least weekly. After stabilization, the interval between INRs can be increased from weekly to biweekly, up to but not beyond 4 weeks.

A goal INR target of 2.5 is recommended for the majority of patients who are kept on long-term anticoagulation. Patients who have recurrent VTE on adequate anticoagulation with coumadin may require a higher target INR (e.g. 3.0). One study suggested protection against recurrence in patients who were initially treated for 6 to 12 months at the target INR of 2.5, then treated to an INR range of 1.5 to 2.0. However, a recent study comparing long-term anticoagulation either at INR 2.5 versus INR 1.5 to 2.0 showed greater protection against recurrence with the higher target INR of 2.5.

Anticoagulation clinics and computerized dosing programs have helped assist in the management and monitoring of patients on warfarin therapy. These areas of anticoagulation are evolving at this time.

Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on establishing and maintaining anticoagulation clinics.

Supporting evidence is of classes: A, C, R

## Long-Term Complications

Long-term complications for patients treated for DVT include recurrent VTE, postphlebitic syndrome, and bleeding while on anticoagulation therapy. There is a high recurrence rate (10% to 15% per year) of thromboembolic disease in patients with idiopathic DVT. Patients should be counseled when discontinuing warfarin to watch for and report signs of recurrence immediately. Ambulatory exercise programs are unlikely to exacerbate symptoms and may result in improved leg muscle flexibility.

Postphlebitic syndrome is characterized by symptoms of heaviness of the leg, fatigue, and pain with findings of dependent edema, skin pigmentation, and venous varicosities. It can be associated with long-term sequelae of subcutaneous fibroses, chronic ulceration, and recurrent infections. It appears that most of the sequelae of postphlebitic syndrome can be attributed to the loss of valvular function. One prospective study revealed that within 2 years of a DVT there was a severe hemodynamic impairment (similar to that seen in established postphlebitic limbs) in one-fifth of patients with calf DVT, and in up to one-half of patients with more extensive proximal DVT. Symptoms were worse after major DVT involving proximal vessels.

Evidence supporting this recommendation is of classes: C, D, R

## Look for Malignancy?

Some patients who present with idiopathic DVT may have occult malignancy. However extensive work-ups in asymptomatic patients beyond appropriate cancer screening have not shown benefit.

In patients with known cancer, risk of DVT is increased. In patients who have idiopathic DVT there may be cancer present at the time of presentation in 3% to 12% of cases.

Evidence supporting this recommendation is of classes: B, C

Thrombophilia

Certain patients should be tested for thrombophilia. This testing should be done 2 weeks after discontinuation of anticoagulation. (See the original guideline document for laboratory test values prevalent in patients with DVT). The work group recommends consideration be given to a discussion with a thrombophilia expert for:

- Patients who have recurrent thromboembolic disease
- Patients with first idiopathic DVT who:
    - Are less than 50 years of age
    - Have a family history of VTE among one or more first-degree relatives
    - Have an unusual site of spontaneous thrombosis
    - Have massive venous thrombosis

Evidence supporting this recommendation is of class: R

Activity Level

There is no evidence that restriction of activity is of benefit nor is there evidence to determine the appropriate activity level. The physician needs to be guided by individual patient circumstance, including pain and swelling.

Ambulatory exercise programs are unlikely to exacerbate symptoms and may result in improved leg muscle flexibility.

Evidence supporting this recommendation is of classes: A, C

69. Other Therapies

Key Points:

- Direct thrombin inhibitors have been used to treat HIT successfully.
- Thrombolytic therapy results in a more rapid clot resolution but does not significantly reduce mortality or risk of recurrent PE.

Inferior Vena Cava (IVC) Filters

Treatment is required due to risk of mortality. Accepted indications for inferior vena caval interruption include:

- Patients with PE or proximal DVT and contraindications to anticoagulation
- Progressive thromboembolism, despite adequate anticoagulation, and
- Patients with underlying pulmonary hypertension in whom a PE would likely be fatal.

Consultation with a specialist is strongly recommended prior to placement of a filter, as long-term sequelae of filter placement include increased risks of recurrent DVT and PE.

IVC filter is the procedure of choice in patients with a contraindication or complication of anticoagulation, who are at high-risk for proximal vein thrombosis, who experience recurrent thromboembolism despite adequate anticoagulation, who have chronic recurrent PE with pulmonary hypertension, or who are undergoing pulmonary embolectomy or pulmonary endarterectomy.

Multiple filter types are available, and all are effective in preventing PE. The Greenfield filter has the longest practical usage for IVC.

Evidence supporting this recommendation is of classes: A, C, R

Serial Ultrasound in Calf DVT

Serial ultrasound (e.g., at 3 and 7 days) may be useful to evaluate for propagation of thromboses in two groups of patients:

- Patients with a positive diagnosis of a calf thrombosis, but contraindications to anticoagulation therapy
- Patients with clinical suspicion of calf thrombosis, but initial negative ultrasound. In general, patients with symptomatic calf DVT who do not have contraindications to anticoagulation will do better if treated similar to those with a proximal DVT.

It is safe to withhold anticoagulation in patients with whom serial compression ultrasound is negative over five to seven days, if the initial study includes the femoral vein, the popliteal fossa, and scan to the trifurcation of the calf veins.

Although serial compression ultrasound testing is safe, it is often inconvenient for patients and healthcare providers, and may not be cost-effective. When patient follow-up cannot be guaranteed, serial compression ultrasound protocols should not be utilized.

Evidence supporting this recommendation is of classes: A, B, C, D, R

Treatment of Heparin-Induced Thrombocytopenia (HIT)

Patients developing HIT while on heparin therapy should be taken off all UFH and LMWH. Direct thrombin inhibitors have been used to treat HIT successfully. Direct thrombin inhibitors approved for the treatment of HIT include lepirudin (Refludan®), argatroban (Acova®), and bivalirudin

(Angiomax®). Direct thrombin inhibitors must be administered by continuous IV infusion necessitating hospitalization. Direct thrombin inhibitor therapy must be monitored by measuring the activated partial thromboplastin time (aPPT).

Please refer to the NGC summary of ICSI's Anticoagulation Therapy Supplement for more information on HIT.

Evidence supporting this recommendation is of class: R

Intravenous (IV) Thrombolytic Therapy

Lytic therapy has been used in patients with extensive iliofemoral disease who demonstrate evidence of vascular compromise (phlegmasia). Lytic therapy has been touted as potentially reducing the long-term postphlebitic consequences of proximal DVT through early thrombolysis, restoration of patency, and preservation of venous valve function. When utilized, catheter-directed lytic therapy is preferred over systemic lytic therapy. This therapy has been suggested as a means of reducing the incidence of post-thrombotic syndrome. However, long-term randomized studies comparing this therapy to standard anticoagulation have not been performed. Management should be individualized and is most appropriate for patients with massive iliofemoral thrombosis. Consultation with a specialist is strongly recommended prior to initiation of lytic therapy.

Thrombolytic therapy results in more rapid clot resolution, but it does not significantly reduce mortality or the risk of recurrent PE in hemodynamically stable patients. Pooled data shows thrombolytic therapy has an increased incidence of major hemorrhage and intracranial hemorrhage as compared to UFH therapy alone. Elevated diastolic blood pressure is a risk factor for intracranial hemorrhage.

Evidence supporting this recommendation is of classes: A, D, M, R

Surgical Thrombectomy

In a highly select group of patients, surgical venous thrombectomy has been utilized. These patients typically have extensive venous thrombosis and have contraindications for anticoagulation and lytic therapy. Surgical thrombectomy has historically been utilized to reduce acute symptomatology in patients with iliofemoral thrombosis and was touted to reduce the risk of postphlebitic syndrome development. Management should be individualized. The morbidity and mortality associated with this surgical procedure deems it be a procedure of last choice.

Evidence supporting this recommendation is of class: D

Definitions:

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

Class D:

- Cross-sectional study
- Case series
- Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

Class R:

- Consensus statement
- Consensus report
- Narrative review

Class X:

- Medical opinion

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

### CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided in the original guideline document for:

- Deep Vein Thrombosis (DVT) Diagnosis
- Pulmonary Embolism (PE) Diagnosis
- V/Q Lung Imaging
- Venous Thromboembolism (VTE) Treatment

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

In addition, key conclusions contained in the Work Group's algorithm are supported by a grading worksheet that summarizes the important studies pertaining to the conclusion. The type and quality of the evidence supporting these key recommendations (i.e., choice among alternative therapeutic approaches) is graded for each study.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Prevention of progression or recurrence of thromboembolic disease
- Reduced risk of complications from anticoagulation therapy
- Improved quality of care and cost-effectiveness of the diagnosis and treatment of venous thromboembolism

## POTENTIAL HARMS

### Diagnosis

The risks associated with a misdiagnosis of pulmonary embolism (PE) are typically more severe than those associated with a misdiagnosis of deep vein thrombosis (DVT). Higher negative predictive values are required to safely use D-dimer to exclude pulmonary embolism.

### Treatment

- Patients on unfractionated heparin (UFH) or low molecular weight heparin (LMWH) therapy who have bleeding, thrombocytopenia, or osteoporosis may require individual adjustments in therapy. Heparin-induced thrombocytopenia (HIT) should be suspected if the platelet count drops 50% or more from baseline labs.
- Patients on warfarin therapy who experience bleeding, skin necrosis, or who become pregnant may require individual adjustments in therapy.
- The development of a complication attributable to anticoagulation requires action by the health care team. Sometimes, as with heparin-induced thrombocytopenia, the drug must be discontinued. The most common complication, bleeding, may require a dosage adjustment, discontinuation of the drug, or further evaluation in the setting of gastrointestinal or genitourinary bleeding. Specific actions are best determined in a case-by-case basis by the clinician, who can appropriately weigh the risks and benefits of continued anticoagulation therapy and who can take into account the timing of the complication.
- Refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) Anticoagulation Therapy Supplement for more information on potential complications of anticoagulation therapy.
- Thrombolytic therapy has an increased incidence of major hemorrhage and intracranial hemorrhage as compared to UFH therapy alone.
- The morbidity and mortality associated with surgical thrombectomy deems it to be a procedure of last choice.

### Long-Term Complications

Long-term complications for patients treated for deep vein thrombosis include recurrent venous thromboembolism, postphlebitic syndrome, and bleeding while on anticoagulation therapy. Postphlebitic syndrome is characterized by symptoms of heaviness of the leg, fatigue and pain with findings of dependent edema, skin pigmentation and venous varicosities. Patients should be counseled when discontinuing warfarin to watch for signs of recurrence and report them immediately.

# CONTRAINDICATIONS

## CONTRAINDICATIONS

### Contraindications to Anticoagulation

Absolute contraindications would include patients who have active severe hemorrhage or recent intracranial hemorrhage. Relative contraindications include: recent or imminent surgery, trauma, anemia (hematocrit less than 30), renal disease, history of gastrointestinal hemorrhage, active peptic ulcer disease, and liver disease.

These patients require more intense monitoring for bleeding complications if given anticoagulation therapy. If not treated with anticoagulation therapy, serial ultrasounds for untreated calf deep vein thrombosis (DVT), or inferior vena cava (IVC) filters for proximal deep vein thrombosis are indicated. Please refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) Anticoagulation Therapy Supplement for more information on contraindications to anticoagulation.

### Known History of Heparin-Induced Thrombocytopenia (HIT)

Patients with heparin-induced thrombocytopenia should not be treated with either unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH). Direct thrombin inhibitors have been used successfully in this circumstance (see Annotation #69). Please refer to the NGC summary of the ICSI Anticoagulation Therapy Supplement for more information on heparin-induced thrombocytopenia.

### Pregnancy

In pregnancy, warfarin (Coumadin®) is contraindicated because it crosses the placenta and is associated with embryopathy, central nervous system (CNS) abnormalities, and neonatal bleeding. Subcutaneous UFH, twice daily, has been the standard therapy in pregnancy. Low molecular weight heparin has shown no increased fetal complication, and was shown to have fewer bleeding complications than UFH. Anticoagulation will need to continue 4 to 6 weeks after delivery because the postpartum period is itself a high-risk time for thrombosis.

Please refer to the NGC summary of the ICSI's Anticoagulation Therapy Supplement for more information on anticoagulation therapy during pregnancy.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
- This clinical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

### IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Clinical Algorithm
Pocket Guide/Reference Cards
Quality Measures

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

### RELATED NQMC MEASURES

- Venous thromboembolism (VTE): percentage of adult patients treated for VTE who have been assessed for the need for graded compression stockings.
- Venous thromboembolism (VTE): percentage of adult patients who have a high clinical pretest probability for pulmonary embolism (PE) who received low molecular weight heparin (LMWH) during evaluation.
- Venous thromboembolism (VTE): percentage of adult patients receiving heparin therapy for VTE who have a baseline platelet count before starting heparin, and then a platelet count every other day for at least the first 3 days of therapy.
- Venous thromboembolism (VTE): percentage of adult patients suspected of deep vein thrombosis (DVT) who have leg duplex ultrasound with compression performed despite a low clinical pretest probability and a negative D-dimer test.

- Venous thromboembolism (VTE): percentage of patients diagnosed with VTE who meet the criteria for low-molecular-weight heparin (LMWH) and for whom LMWH is used.
- Venous thromboembolism (VTE): percentage of low-molecular-weight heparin (LMWH)-eligible patients with deep vein thrombosis (DVT) treated in an outpatient setting.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better
Living with Illness

### IOM DOMAIN

Effectiveness
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Feb. 91 p. [202 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

1998 Jun (revised 2006 Feb)

### GUIDELINE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

### GUIDELINE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and

Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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## GUIDELINE COMMITTEE

Cardiovascular Steering Committee

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

In the interest of full disclosure, Institute of Clinical Systems Improvement (ICSI) has adopted a policy of revealing relationships work group members have with companies that sell products or services that are relevant to this guideline topic. The reader should not assume that these financial interests will have an adverse impact on the content of the guideline, but they are noted here to fully inform readers. Readers of the guideline may assume that only work group members listed below have potential conflicts of interest to disclose.

Bruce Burnett, MD is a member of the speakers bureau for Aventis, BMS, and Astra Zeneca; a consultant for Aventis, Astra Zeneca, and Glaxo SmithKline; receives research support from Astra Zeneca.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Venous thromboembolism. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Apr. 99 p.

## GUIDELINE AVAILABILITY

Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

## AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Venous thromboembolism. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement, 2006 Feb. 1 p. Electronic copies: Available from the Institute for Clinical Systems Improvement (ICSI) Web site.
- ICSI pocket guidelines. May 2005 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2005. 362 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

## PATIENT RESOURCES

None available

## NGC STATUS

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